

# Effect of laparoscopic ovarian drilling on ovulation rate in women with clomiphene resistant polycystic ovarian syndrome

Sana Ansari, Reena Yadav, Nishtha Jaiswal

**Corresponding author:** Dr Nishtha Jaiswal, Associate Professor, Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and SSK Hospital, New Delhi, Delhi, India; Email : nishtha.amu@gmail.com

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## ABSTRACT

**Background:** Laparoscopic ovarian drilling (LOD) is a surgical treatment that can stimulate ovulation in women diagnosed with polycystic ovarian syndrome (PCOS) and especially those with resistance to clomiphene citrate (CC). **Objective:** To observe the effect of LOD on ovulation rate in women with PCOS. **Methods:** The study included thirty CC resistant PCOS women between 20-35 years of age, trying for conception, with patent bilateral fallopian tubes and male factor infertility ruled out. Hormone levels including serum LH, FSH and testosterone were tested on day 2/3 of menstrual cycle before and 1 month after LOD. Patients underwent LOD in between 5<sup>th</sup> -9<sup>th</sup> day of the cycle. During the procedure each ovary was drilled using monopolar cautery of 40 W of power at 4 sites, 4mm deep, for 4 seconds. Spontaneous ovulation rate was noted by follicular monitoring done by transvaginal sonography following LOD in the next two menstrual cycles. **Results:** It was observed that serum testosterone levels reduced from  $46.56 \pm 24.06$  ng/dl before LOD to  $35.02 \pm 19.85$  ng/dl after LOD and 80% PCOS women ovulated after ovarian drilling (i.e., 24 out of 30 cases). 8 women conceived following LOD making the cumulative pregnancy rate of 33.33%. **Conclusions:** LOD induces ovulation in PCOS women resistant to CC due to decreasing testosterone levels as seen in this study. So prior to initiation of gonadotropin therapy for CC resistant PCOS, LOD may be used as an alternative treatment in such cases.

**Keywords:** Ovarian drilling, laparoscopy, clomiphene resistance, PCOS, pregnancy.

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting 5-10% of reproductive age women and at least 75% of cases with anovulatory infertility<sup>1</sup>. PCOS is diagnosed based on the 2003 ESHRE (Rotterdam criteria)<sup>2</sup> - 1) Clinical and biochemical evidence of increased androgen; 2) Oligomenorrhea or amenorrhea; 3) Ultrasound evidence of polycystic ovaries (12 subcortical follicles of 2-9 mm in diameter with dense stroma and/or increased ovarian volume (more than 10 ml) and ruling out other causes (congenital adrenal hyperplasia, androgen secreting tumors, Cushing syndrome). A single ovary meeting these criteria is sufficient to affix the polycystic

ovarian morphology. The presence of at least two of the three criteria is sufficient to diagnose PCOS.

Chronic anovulation is one of the leading cause of infertility. The first line drug for anovulatory infertility in PCOS is clomiphene citrate (CC), a selective oestrogen receptor modulator<sup>3</sup>. It is typically administered in an empiric incremental fashion to identify the lowest effective dosage (50-150 mg daily for 5 days, beginning on cycle day 2 -6<sup>4</sup>). CC resistance refers to anovulation even after three cycles of ovulation induction with 150 mg of CC<sup>3</sup>. Approximately 20% of patients prove refractory to clomiphene treatment, most of those having severe

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hyperandrogenism or obesity<sup>5</sup>. Treatment options in CC resistant PCOS include gonadotrophins or laparoscopic ovarian drilling (LOD). However, gonadotrophins is an expensive treatment and has an additional side effects of ovarian hyperstimulation syndrome (OHSS) and multifetal pregnancy.

Ovarian drilling induces ovulation in PCOS women and especially those resistant to clomiphene citrate<sup>3</sup>. Surgical therapy with LOD may reduce the need for medical ovulation induction, or may facilitate its usefulness<sup>6</sup>. The present study was undertaken to observe the effect of LOD on ovulation rate in women with PCOS.

**Material and methods**

An observational study was conducted in the department of obstetrics and gynaecology at Lady Hardinge Medical College and SSK Hospital from November 2018 to March 2020. A prior approval from the institutional ethical committee and informed consent was taken. 30 CC resistant PCOS women were taken as sample size. Women between 20-35 years age group, trying for conception, clinically diagnosed as CC resistant PCOS were enrolled in the study. Other inclusion criteria were normal hysterosalpingography and no male factor infertility. Hormone levels including serum LH, FSH and testosterone were tested on 2<sup>nd</sup> or 3<sup>rd</sup> day of menstrual cycle before and 1 month after LOD, which was done in between 5<sup>th</sup>-9<sup>th</sup> day of menstrual cycle. During the procedure each ovary was drilled using monopolar cautery of 40 W power at 4 sites, 4mm deep, for 4 seconds. One month after LOD, same hormone levels were again tested on 2<sup>nd</sup> or 3<sup>rd</sup> day of menstrual cycle. Spontaneous ovulation rate was noted by follicular monitoring done by transvaginal sonography following LOD in 2 successive menstrual cycles.

Statistical analysis: Collected data was entered in MS-EXCEL and then analysed using MS-EXCEL and SPSS latest version. Basic statistical characteristics of quantitative data were expressed by using mean and standard deviation. Difference of mean was tested by student t -test. Percentage and proportion were used for calculation for qualitative data. Association between categorical variables was done using chi-square test or fisher exact test. A p value of <0.05 was taken as significant.

**Results**

Table 1 shows demographic data of cases. Age group of women varied from 26-35 yrs. Mean age was 28.47 ± 1.80 years and mean BMI was 27.94 ± 5.90 kg/m<sup>2</sup>. Infertility

period of cases was range between 3-11 years with the mean of 6.23 ± 2.47 years. Mean waist hip circumference ratio was 0.9 ± 0.05, which was raised.

**Table 1: Demographic data of cases (N=30)**

Variables	Mean ± SD
Age (years)	28.47 ± 1.80
BMI (kg/ m <sup>2</sup> )	27.94 ± 5.90
Duration of infertility (years)	6.23 ± 2.47
Waist hip circumference ratio (WC/HC)	0.9 ± 0.05

As shown in table 2, out of 30 cases, 23 (76.7%) cases had oligomenorrhea and 7 (23.3%) cases had amenorrhea. Hirsutism was present in 17 (56.7%) cases and absent in 13 (43.3%) cases. Acne was present in 3 (10%) cases and acanthosis was present in 9 (30%) cases.

**Table 2: Clinical parameters (N=30)**

Clinical parameters	Number	Percentage
Menstrual cycle		
-Oligomenorrhea	23	76.7
-Amenorrhea	7	23.3
Hirsutism	17	56.7
Acne	3	10
Acanthosis nigricans	9	30

Table 3 shows comparison of mean LH value before (11.80 ±7.25) and after LOD (10.6 ± 5.91 IU/L), the difference was found to be statistically insignificant (p value= 0.132). Mean FSH value before LOD was 6.30 ± 1.08 IU/L and after LOD was 5.83 ± 1.53 IU/L. This difference was found to be statistically significant (p value= 0.025). Mean LH/ FSH value before (1.83 ± 1.03) and after LOD (2.11 ± 2.20) was found to be statistically insignificant (p value= 0.439). The difference between mean testosterone levels before (46.56 ±24.06 ng/dl) and after LOD (35.02 ± 19.85 ng/dl) was found to be statistically significant (p value< 0.001).

Before LOD, all 30 cases were anovulatory (100%). Post

**Table 3: Hormone profile pre and post LOD (N=30)**

Hormone	Pre LOD (Mean ± SD)	Post LOD (Mean ± SD)	P value
LH (IU/L)	11.8 ±7.25	10.62 ± 5.91	0.132
FSH (IU/L)	6.3 ± 1.08	5.83± 1.53	0.025
LH/FSH	1.83 ± 1.03	2.11 ± 2.2	0.439
Testosterone (ng/dl)	46.56 ± 24.06	35.02 ± 19.85	<0.001

LOD, out of 30 cases, 24 (80%) women ovulated spontaneously. However, rest 6 (20%) cases had anovulatory cycles. Total 8 women out of 24 cases conceived during the

**Table 4: Ovulation and pregnancy rate post LOD**

Categories	Number	Percentage
Ovulation rate (N=30)	24	80 %
Pregnancy rate (N=24)	8	33.33 %

study period. Therefore, cumulative pregnancy rate after 1<sup>st</sup> and 2<sup>nd</sup> menstrual cycle was 8.3 % (2 out of 24) and 25% (6 out of 24) respectively. Cumulative pregnancy rate after the extended follow up at 8 months after LOD was 33.33% (table 4).

## Discussion

In our study, amongst the 30 patients with CC resistant polycystic ovaries, ovulation occurred in 24 patients (80%) 1 month after LOD. The remaining rest 20% of patients had anovulatory cycles. A study done by Amer et al in 2004 showed that among the 30 patients with CC resistant polycystic ovary, ovulation rate was 78%<sup>7</sup>. This is similar to the findings seen in our study.

The cumulative pregnancy rate was 2/24 (8.3%), 6/24 (25%) and 8/24 (33.33%) 1 month, 2 months and 8 months after LOD respectively in our study. Poujade et al included 74 CC resistant polycystic ovary women and found conception in 47 (63%) patients but this was within 11 months after LOD<sup>8</sup>. The higher cumulative conception rate in their study could be explained by a longer period of follow up. Similarly, Debras et al<sup>9</sup> found that in 289 women with a mean follow-up of 28.4 months, pregnancy was obtained in at least 137 (47.4%) women after a drilling, and 71 (51.8%) of these pregnancies were spontaneous, 48 (16.6%) women achieved at least two pregnancies after drilling, and 27 (56.3%) of these were spontaneous. The predictive factors for effectiveness were a normal body mass index (BMI), an infertility period of less than three years, an AFC of less than 50, and an age of less than 35 years.

In our study the serum testosterone levels had a statistically significant reduction ( $p$  value < 0.001) when compared pre LOD ( $46.56 \pm 24.06$  ng/dl) and post LOD ( $35.02 \pm 19.85$  ng/dl). This finding is similar to a study by Salem et al 2017 which also showed significant ( $p$  value = 0.05) reduction of testosterone levels post ovarian drilling (from  $2.61 \pm 1.15$  pre LOD to  $1.61 \pm 0.6$  post LOD)<sup>10</sup>. This can be explained by destruction of androgen producing ovarian stroma during LOD. It is known that increasing serum levels of testosterone and/or increasing free androgen index (FAI) are associated with a statistically significant reduction of the chances of success of LOD. Furthermore, a subgroup of PCOS women with marked hyperandrogenism (testosterone  $\geq 4.5$  nmol/l, FAI  $\geq 15$ ) appeared to be resistant to LOD. Gjonnaess et al<sup>11</sup> in 1994 found that women with low levels of sex hormone binding globulin (i.e. high levels of free testosterone), whether they were of normal weight or overweight, were less likely to respond to LOD. Our study demonstrated that there was a reduction in serum testosterone levels post LOD which could have facilitated conception.

The risks of LOD are ovarian adhesion formation, reduced ovarian reserve and premature ovarian failure<sup>12-14</sup>.

These complications were not seen in our cases which may be because of following precautions taken during LOD: irrigation with saline after electrocautery, avoiding the tubo-ovarian junction, keeping a maximum cautery depth of 4 mm at 4 sites for 4 seconds only, using a minimum power of 40 watts and achieving adequate haemostasis. Laparoscopic treatment is increasingly being recommended as an early treatment option for women with clomiphene resistant PCOS. The reduction in serum androgen levels after LOD is reported to be the main mechanism by which reproductive outcome is improved<sup>15</sup>. Our study also provides support to the fact the LOD is an effective treatment modality for clomiphene resistant PCOS.

## Conclusion

LOD induces ovulation in PCOS women resistant to CC due to decreasing testosterone levels as seen in this study. So prior to initiation of gonadotropin therapy for CC resistant PCOS, ovarian drilling may be used as an alternative treatment in such cases.

**Conflict of interest:** None. **Disclaimer:** Nil.

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- Sana Ansari <sup>1</sup>, Reena Yadav <sup>2</sup>, Nishtha Jaiswal <sup>3</sup>**  
<sup>1</sup> Senior Resident, Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and SSK Hospital, New Delhi, Delhi, India; <sup>2</sup> Director Professor and Unit Head, Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and SSK Hospital, New Delhi, Delhi, India; <sup>3</sup> Associate Professor, Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and SSK Hospital, New Delhi, Delhi, India.